

Mini-reviews

Two of the mini-reviews in this issue evaluate the laparoscopic approach to urology; one critically appraising laparoscopic nephroureterectomy for upper tract TCC, and the other looking back on the first 10 years of laparoscopic pyeloplasty. They are also a testament to the relationship which has developed between the effects of British urologists in becoming experts in this area, and the outstanding help and supervision given by Inderbir Gill and his team at the Cleveland Clinic. The financial backing for this venture came from the British Urological Foundation, which enthusiastically supports the concept of this preceptorship at the Cleveland Clinic.

Laparoscopic nephroureterectomy for upper tract transitional cell carcinoma: a critical appraisal

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Accepted for publication 5 December 2003

KEYWORDS

laparoscopy, nephroureterectomy, transitional cell carcinoma

INTRODUCTION

As surgical technology and techniques develop a reassessment of treatment strategies is inevitable. Although minimally invasive alternatives hold the promise of decreasing patient morbidity, vigilance must be constant to ensure strict adherence to long-established surgical and oncological principles. TCC of the upper urinary tract is a relatively uncommon disease, representing 5% of all urothelial tumours [1], and which appears to lend itself to minimally invasive management. Although there is a role for ureteroscopic management of small, solitary, low-grade tumours, particularly in patients with impaired renal function or bilateral disease [2], most TCC affecting the upper tract is grade 2 or 3 (18.5–48.2% and 42.5–47%, respectively) [3–5]. As the grade and stage of the disease are closely related, higher grade tumours tend towards muscle invasion and a poorer prognosis. As such, nephroureterectomy (NU) remains the therapy of choice for most patients with upper tract TCC and a normal contralateral renal unit [5–9].

The standard open surgical approach to NU (ONU) with excision of a cuff of bladder uses either one or two large skin incisions. Laparoscopic nephroureterectomy (LNU) was first reported in 1991 by the Washington University Group [10–12], and when compared to ONU has been shown to offer reduced perioperative morbidity, a shorter hospital stay, and a reduced requirement for transfusion [13–15].

Despite these obvious advantages there is rightful concern about the oncological effectiveness of LNU. Given the aggressive nature of the disease and the risk of local recurrence, long-term follow-up data over at least 5 years are necessary to allay this concern. The objectives of this review are to discuss aspects relating to the oncological effectiveness and to examine the outcomes for LNU thus far reported [13,16–27].

Published material was searched for articles reporting outcomes of series of LNU for TCC of the renal pelvis or ureter, using Pubmed (www.ncbi.nlm.nih.gov/PubMed/). In addition, we also hand-searched the abstract books from the most recent major urological conferences to identify data of interest that have so far been presented only as abstracts.

TECHNICAL ASPECTS

The dissection of the kidney for LNU is the same as for radical nephrectomy, which has been well described [28]. Whether the approach is retroperitoneal or transperitoneal depends on the operating surgeon's preference, although most laparoscopic surgeons currently prefer the transperitoneal approach, as it affords greater operating space. A small comparative study from an experienced group recently reported that the operative duration with hand-assistance was shorter by a mean of 1 h (4.9 vs 6.1 h, $P=0.055$), the authors also suggesting that the technique facilitates the learning of the wholly laparoscopic approach [29]. However, other reports of LNU have shown that with experience the operative duration for the laparoscopic procedure can approach that of ONU without the use of hand-assistance [17,18].

More important is whether any of these methods compromise the oncological effectiveness of the operation, as shown by the incidence of positive tumour margins, local recurrence, distant metastases and the long-term survival. In addition, laparoscopic procedures for malignant disease must be scrutinized for evidence of port-site seeding, which has been reported after LNU for TCC [30,31]. As long as basic surgical principles of wide local excision are respected, it may be argued that it is the inherently aggressive nature of the disease rather than the surgical approach adopted that leads to wound recurrence, which has also been reported after ONU [32,33]. Of the criteria that many use to assess the oncological effectiveness of a given surgical procedure, the incidence of positive surgical margins and local recurrence can be determined within a relatively short follow-up and may give an indication of the likely long-term results.

MANAGEMENT OF THE DISTAL URETER AND BLADDER

The surgical goal during NU is complete removal of the entire distal ureter with a bladder cuff. As recurrence at the ureteric orifice is the best recognized of local recurrences after NU it is appropriate to consider the various techniques used to manage the distal ureter and bladder cuff [34]. Preliminary resection of the ureteric orifice with a 'pluck', as described by

Abercrombie *et al.* [35], caused significant concern after reports of tumour seeding into the peritoneum from the open distal end of the ureter [36,37].

The second approach involves initial completion of the laparoscopic nephrectomy and dissection of the ureter distally towards the bladder base. An endoscopic GIA stapler is then used to excise a cuff of bladder with the distal ureter [11]. The specimen is removed intact through a Pfannenstiel or other lower abdominal incision.

The third technique involves transvesical laparoscopic dissection of en bloc bladder cuff and distal ureter with placement of an Endoloop™ tie (US Surgical, Norwalk, CT); retroperitoneal LNU is then completed. Whilst technically challenging this is the only minimally invasive technique that provides complete en bloc removal of the bladder cuff, akin to open surgery [38].

The fourth technique involves completing the nephrectomy laparoscopically with removal of the distal ureter and bladder cuff by a formal open surgical approach.

There is no consensus view on which of the available methods is best for managing the lower end of the ureter either at ONU or LNU. However, there were no significant differences in distal ureteric recurrences in a recent large multi-institutional American and European study when analysed according to the method adopted for removing the distal ureter [23]. This group found that those with multifocal or ureteric tumours had a lower 3-year survival than those with disease in the renal pelvis. As a lower abdominal incision is often used for retrieving the intact specimen, and the oncological effectiveness of an open dissection of the distal ureter (including opening of the bladder if required) is not disputed, adopting this approach in patients with multifocal or ureteric disease is reasonable. Added benefits of this approach include decreased operating time and eliminating the need to reposition the patient.

LYMPHADENECTOMY

An open procedure may allow a more extensive lymphadenectomy during radical NU. However, information about lymph node status is often not provided in reports, being available in only 4% of patients undergoing

either LNU or ONU in the series from Edinburgh [17]. Consequently, the therapeutic role of lymphadenectomy in NU remains unclear and controversial, as it has not been shown to confer clear therapeutic benefit in patients with upper tract TCC [39]. While it can be argued that those patients in need of palliative chemotherapy will be identified earlier by routine extended lymphadenectomy, whether this ultimately confers any overall survival benefit is uncertain.

PERIOPERATIVE OUTCOMES

Twelve series of LNU reporting a total of 396 patients have now been published [13,16–27]. Some of these patients might have been reported in individual series [16–18,22] and in a larger collaborative series [23]; the results are summarized in Table 1.

Notably, of the patients in these series a mean (range) of 42 (23.5–65)% had high-grade TCC (grade 3 or 4) and an additional 38 (24–75)% had moderately differentiated TCC. This may reflect current trends in practice towards the endoscopic management of solitary low-grade tumours, although the pattern of disease was noted in previous series, as long ago as 1976 [3,4]. It is therefore essential that appropriate measures, e.g. endoscopic biopsy, be taken to fully assess this disease before definitive therapy, particularly when endoscopic management is being considered.

In keeping with the described epidemiology of this malignancy, the vast majority of the patients in the reviewed series were in their sixth and seventh decades. In the laparoscopic groups the operative times were 165–462 min, blood loss 199–445 mL, hospital stay 2.3–17 days and follow-up was up to a mean of 35 months.

Seven series reported a retrospective, unrandomized comparison of outcome of LNU with ONU [13,17,18,21,25–27], thus providing an initial basis for comparing the outcome between the surgical approaches. The reported operative duration for LNU was generally longer than for ONU, as may be expected, but there was generally a reduction in blood loss (mean 248 vs 441.6 mL) and a shorter postoperative stay (median 4.1 vs 6.6 days). Of note, two studies [20,26] reported long stays for both LNU and ONU. The explanation provided for this by Hattori

TABLE 1 Published comparative reports of laparoscopic and open nephroureterectomy for upper tract TCC. There were no port-site recurrences in any study.

Variable	Reference											
	[16]	[13]	[17]	[18]	[19]	[20]	[21]	[22]	[23]	[25]	[26]	[27]
Surgical method	L	L/O	L/O	L/O	L	L	L/O	L	L	L/O	L/O	L/O
No. of patients	4	25/17	25/42	42/35	22	5	16/11	25	116	17/17	65/44	34/34
Mean age, years	67.7	69.7/62	68/69.1	71.6/64.3	65	–	71/71	63	68	75/71	66	67
% patients with												
G3	25	28/23.5	52/38	55/46	41	–	31/54	44	42	58/65	–/–	26/38
G2	75	24/47	24/47	24/28	45	–	25/36	32	35	35/35	–/–	59/50
Mean:												
op. duration, min	220	462/234	165/165	222/282	272	234	320/199	329	–	287/240	300/318	233/236
blood loss, mL	–	199/441	–/–	242/696	180	–	288/345	440	–	151/299	445/766	236/427
hospital stay, days	5.7	6.1/12	9.1/10.7	2.3/6.6	4.1	17	3.9/5.1	4	–	2.7/4.2	–/–	13/21
follow-up, months	–	24/24	35/46	11.1/34.4	18	2–8	12/14	>12	25	8.8/23	29/33	13/49
Recurrence, n:												
extravesical local	1	2/0	–/–	0/0	0	0	0/3	1	2	1/4	–/–	0/0
distant	–	2/2	–/–	3/4	2	0	0/1	4	11	0/2	–/–	2/3
Complications, %	–	48/58	16/17	12/29	–	–	19/27	12	–	12/12	–/–	12/12
Disease-related	–	3/3	4/9	1/2	0	0	–/–	2	23	0/2	–/–	–/–
Survival, %:												
metastasis-free												
1 year	–	–	–	–	–	–	–	–	–	–	88/87	
5 years	–	–	–	–	–	–	–	–	–	–	72/75	
Disease-specific												
1 year	–	–	–	–	–	–	–	–	92	–	94/95	
2 years	–	–	–	–	–	–	–	–	87			
5 years	–	–	–	–	–	–	–	–	–	–	91/83	

L, LNU; O, ONU.

et al. [26] was that in South-east Asia patients are reluctant to go home until they are almost completely recovered, which is reflected in a mean stay of 21 days after ONU [28].

These initial series provide evidence that LNU confers reduced morbidity, shorter hospital stay and faster overall recovery. With experience and technical refinement it is possible to obtain operating times comparable to ONU [17,18].

ONCOLOGICAL OUTCOMES

Longer-term outcome analysis evaluating the oncological effectiveness of LNU is perhaps the most important data that has been lacking in the past. Although the mean follow-up in the LNU groups ranges from only a few months to 35 months, in two of the series it was possible to calculate disease-specific survival rates at 2 and 5 years [23,26]. The absence of any port-site recurrences is likely to be a consequence of improvements

in technique, in particular the use of impermeable entrapment sacks to permit intact removal of the specimen. It is the opinion of the authors that morcellation of these TCC specimens must be avoided, given the inherently aggressive nature of this malignancy.

The collaborative study of 116 patients undergoing LNU by El Fettouh *et al.* [23] reported disease-specific survivals of 92% and 87% at 1 and 2 years, respectively. Hattori *et al.* [26] provided a longer-term follow-up of a group of 65 patients undergoing LNU compared with a group of 44 undergoing ONU. Reported 1- and 5-year metastasis-free survival rates between the groups were similar at 88% and 87%, and 72% and 75%, respectively. Disease-specific survival calculated from their data indicates 1- and 5-year survival rates of 94% and 91% in the LNU group, which compare well to those in the ONU group of 95% and 83%. These survival rates also compare well to the survival data produced by Hall *et al.* [4], who found that

stage of disease was closely related to survival, those with Ta disease tending to have an excellent long-term outcome. Finally, in all of these series there were very few reports of extravesical recurrences, with no apparent differences between the surgical groups.

SUMMARY

When assessed by the criteria of patient morbidity, hospital stay and overall recovery, LNU is superior to ONU. When assessed by the criteria of oncological effectiveness outlined above, the reviewed reports suggest that LNU is comparable with ONU as a definitive treatment for upper tract TCC. With intact specimen removal there is no apparent increase in positive surgical margins, or local or port site recurrences. Data on longer-term survival are also comparable between the groups, with most deaths occurring from metastasis, which reflects the aggressive nature of the disease. The method chosen to remove the distal ureter is important and

should follow established principles of oncological surgery.

In conclusion, LNU appears to be a safe therapy for patients with upper tract TCC. The shorter hospital stay and faster overall recovery will obviously be attractive to the patient, but more importantly the longer-term cancer control and survival appears to be equivalent to that after ONU.

ACKNOWLEDGEMENTS

This review was made possible by the BUF/BAUS funded programme of Laparoscopic Preceptorships at the Cleveland Clinic Foundation.

CONFLICT OF INTEREST

None declared.

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Abbreviations: (O)(L)NU; (open), (laparoscopic) nephroureterectomy.